PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 31757PC01	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/DK2004/000062	International filing date *(day/month/year)* 30.01.2004	Priority date *(day/month/year)* 30.01.2003

International Patent Classification (IPC) or national classification and IPC
A61K38/17, A61P35/00, C07K14/47, C07K16/18, G01N33/574, G01N33/68

Applicant
SURVAC A/S

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 11 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 4 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
01.12.2004	24.02.2005

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/DK2004/000062

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-57 as originally filed

Sequence listings part of the description, Pages

1-20 as originally filed

Claims, Numbers

1-34 received on 03.12.2004 with letter of 01.12.2004

Drawings, Sheets

1/17-17/17 as originally filed

☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-34 (all in part and insofar as applicable)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-34 (all in part and insofar as applicable)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☒ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-34 (all in part and insofar as applicable)
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-34 (all in part and insofar as applicable)
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-34 (all in part and insofar as applicable)
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☒ contained in the international application as filed

   ☒ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item III.

1. **AMENDMENTS**

1.1 Amended claims, especially independent claims 1, 29 and 34, are not limited to the peptide of SEQ ID NO: 1 and as such, the subject-matter of the amended set of claim now relates to subject-matter for which an international search has not been established. The IPEA cannot give an opinion on non-searched subject-matter (Rule 66.1(e) PCT). The search is the responsibility of the ISA under Chapter I of the PCT, the procedure before the ISA is closed and that there is no provision in the PCT for a review of or an appeal against the findings of the ISA by the IPEA.

1.2 Thus, the present opinion is given only for the claims relating to subject-matter which was searched, as indicated in the International Search Report and as follows:

1.2.1 **Invention 1** (claims 1-34 all in part and insofar as applicable): An MHC Class I (**HLA-A2**)-restricted epitope peptide derived from survivin consisting of **SEQ ID NO: 1 (FLKLDRERA, survivin$_{101-109}$ peptide)** ; A composition or pharmaceutical composition comprising such peptide; A complex of such peptide and a Class I HLA molecule; A method for detecting the presence of survivin using such complex; Antibodies binding to such peptide; uses of such peptide or composition for the preparation of a medicament for the treatment of cancer.

Re Item V.

2. The following **documents** are referred to in this communication:

D1 : ANDERSEN MADS HALD ET AL: "Identification of a cytotoxic T lymphocyte response to the apoptosis inhibitor protein survivin in cancer patients" CANCER RESEARCH, vol. 61, no. 3, 1 February 2001 (2001-02-01), pages 869-872, XP002283853 ISSN: 0008-5472

D2 : ANDERSEN MADS HALD ET AL: "Spontaneous cytotoxic T-cell responses against survivin-derived MHC class I-restricted T-cell epitopes in situ as well as ex vivo in

cancer patients" CANCER RESEARCH, vol. 61, no. 16, 15 August 2001 (2001-08-15), pages 5964-5968, XP002283854 ISSN: 0008-5472

D3 : SCHMITZ MARC ET AL: "Generation of survivin-specific CD8+ T effector cells by dendritic cells pulsed with protein or selected peptides" CANCER RESEARCH, vol. 60, no. 17, 1 September 2000 (2000-09-01), pages 4845-4849, XP002283855 ISSN: 0008-5472

D4 : HIROHASHI YOSHIHIKO ET AL: "An HLA-A24-restricted cytotoxic T lymphocyte epitope of a tumor-associated protein, survivin." CLINICAL CANCER RESEARCH : AN OFFICIAL JOURNAL OF THE AMERICAN ASSOCIATION FOR CANCER RESEARCH. JUN 2002, vol. 8, no. 6, June 2002 (2002-06), pages 1731-1739, XP002283856 ISSN: 1078-0432

D5 : FORTUGNO PAOLA ET AL: "Survivin exists in immunochemically distinct subcellular pools and is involved in spindle microtubule function" JOURNAL OF CELL SCIENCE, vol. 115, no. 3, 1 February 2002 (2002-02-01), pages 575-585, XP002283857 ISSN: 0021-9533

3. NOVELTY

3.1 MHC Class I-restricted peptides derived from survivin have been disclosed in the prior art (D1; see e.g. Table 1, D2-D5).

3.2 Document D1 discloses HLA-A2-specific survivin peptides: Sur1- Sur 10, Sur1L2, Sur1M2 (Table 1) which are identical to HLA-A2-specific survivin peptides claimed in present application (SEQ ID NO: 10, 12-17, 1-5). D1 also discloses specific CTL responses against said peptides, affinity values for the binding of said peptides to Class I HLA molecules and suggests the uses of such peptides in vaccination and cancer therapy and diagnosis.

3.3 Document D2 discloses HLA-binding survivin peptides: Sur1 (LTLGEFLKL), Sur9 (ELTLGEFLKL) and Sur1M2 (D2, Table 1), identical to HLA-A2-specific survivin peptides claimed in present application (SEQ ID Nos: 10, 3 and 5 of the present application, respectively), and the generation of CTL responses by said peptides. D2 discloses HLA-A2/peptide complexes which were multimerised, and their use in

detection of survivin reactive cells in tumor tissue. D2 suggests uses of such survivin peptides for peptide-based anticancer vaccines in combination with conventional cancer chemotherapy.

3.4 Document D3 discloses HLA-binding survivin peptide ELTLGEFLKL (see e.g. page 4847, left-hand column, paragraph 2 to page 4849, left-hand column, paragraph 4). Said peptide is identical to SEQ ID NO: 3 of the present application. D3 discloses the generation of CTL responses by said peptide and suggests uses thereof for peptide-based anticancer vaccines.

3.5 Document D4 discloses an HLA-A24 restricted CTL epitope of survivin-2B (splice variant found in tumors) survivin2B80-88 (D4, Abstract, page. 1733, left-hand column, paragraph 2, figures 1, 3). D4 also discloses other survivin peptides; e.g. survivin85-93 (AFLSVKKQF; identical to SEQ ID NO: 48 of the application over 9 amino acids) and survivin 92-101 (QFEELTLGEF; identical to SEQ ID NO: 27 of the application).

3.6 D5 discloses polyclonal antibodies against survivin epitopes Ala3-Ile19, Met 38-Thr48, Pro47-Phe58 and Cys57-Trp67. These epitopes overlap with survivin peptides in the present application and the antibodies will bind to said peptides.

3.7 Although pharmaceutical compositions comprising a combination of two or more MHC class I-restricted epitope peptides derived from survivin, each interacting specifically with a different HLA molecule and having the characteristics indicated in claim 1 were known in the art, none of the prior art documents discloses such a composition comprising a peptide consisting of **FLKLDRERA** (SEQ ID NO: 1; invention 1).

3.8 Thus, the subject-matter of independent claim **1**, insofar as related to a pharmaceutical composition comprising a combination of two or more MHC class I-restricted epitope peptides derived from survivin, wherein one of said epitope peptides is a peptide consisting of **FLKLDRERA** (SEQ ID NO: 1; invention 1), is new in the sense of Article 33(2) PCT.

3.9 The subject-matter of independent claim **29**, insofar as related to a multiepitope vaccine comprising a combination of two or more MHC class I-restricted epitope peptides derived from survivin, wherein one of said epitope peptides is a peptide consisting of **FLKLDRERA** (SEQ ID NO: 1; invention 1), is new in the sense of Article 33(2) PCT.

3.10 Dependent claims **2-28, 20-33** and claim **34** are also new in the sense of Art. 33 (2) PCT, insofar as they relate to the peptide consisting of **FLKLDRERA** (SEQ ID NO: 1; invention 1).

4. INVENTIVE STEP

4.1 Many MHC Class I-restricted peptides derived from survivin have been disclosed in the prior art (D1-D5). For instance, D1 discloses HLA-A2-specific survivin peptides and specific CTL responses against said peptides, affinity values for the binding of said peptides to Class I HLA molecules and suggests the uses of such peptides in vaccination and cancer therapy and diagnosis (see e.g. D1, Table 1, examples).

4.2 In the light of the above mentioned prior art, the problem of the present application can be summarized as providing further compositions comprising MHC Class I-restricted peptides derived from survivin for use in vaccination and cancer therapy. The solution provided in claim 1 is a pharmaceutical composition comprising a combination of two or more MHC class I-restricted epitope peptides derived from survivin, each interacting specifically with a different HLA molecule and having the characteristics indicated in claim 1.

4.3 Pharmaceutical compositions comprising MHC class I-restricted epitope peptides derived from survivin, having the characteristics indicated in claim 1 were known in the art (D1-D5). From the prior art it is obvious that different peptide are specific for different HLA-alleles in the population. It is considered as a standard knowledge of a skilled person, that in order to formulate a composition suitable for a population, epitopes of any given antigen which are able to bind to the different HLA molecules in the population should be used for vaccination. Thus, a general claim where two or

more MHC class I-restricted epitope peptides derived from survivin, each interacting specifically with a different HLA molecule and having the characteristics indicated in claim 1 (i-iii) are combined in a pharmaceutical composition, does not appear to involve an inventive step in view of Art. 33 (3) PCT.

4.4 However, since it was not obvious or derivable from the prior art that the specific peptide consisting of SEQ ID NO: 1 (FLKLDRERA) would effectively bind to the HLA-A2 molecule (see e.g. present application table 1), a claim to a pharmaceutical composition comprising a combination of two or more MHC class I-restricted epitope peptides derived from survivin, each interacting specifically with a different HLA molecule and having the characteristics indicated in claim 1, wherein one of said epitope peptides is a peptide consisting of **FLKLDRERA** (**SEQ ID NO:** 1; invention 1), would be regarded as inventive in the sense of Art. 33 (3) PCT.

4.5 The same argument applies for independent claims **29** and **34** and dependent claims **2-28, 20-33**.

5. CLARITY, SUPPORT and SUFFICIENCY OF DISCLOSURE

5.1 Claims **1, 29 and 34** do not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. The claims attempt to define the subject-matter in terms of the result to be achieved, which merely amounts to a statement of the underlying problem, without providing the technical features necessary for achieving this result. This applies to points (i), (ii) and especially (iii) of claims 1 and 29.

5.2 In addition, claims 1, 29 and 34 broadly define the subject-matter by functional statements (i) (ii) and (iii), which do not enable a skilled person to determine which technical features are necessary to perform the stated functions. Hence, claim 1, 29 and 34 are not supported by the description as required by Article 6 PCT.

5.3 It appears that since not all possible epitope peptides are suitable for use in pharmaceutical compositions or as a vaccine, it would represent an undue burden for

a skilled person to determine which peptides fall within the scope of claims 1, 29 and 34 and as such, a lack of sufficient disclosure arises within the meaning of Art. 5 PCT.

5.4 The same objections on lack of clarity, support and disclosure (Art. 5, 6 PCT) applies for the subject-matter of dependent claims **2-9, 11, 12, 14-28, 30-33.**

5.5 Claims **10** and **13** define the subject-matter in terms of the sequence of the epitope peptide and as such, the requirements of Art. 5 and 6 PCT are met.

Amended claims

1. A pharmaceutical composition comprising a combination of two or more MHC Class I-restricted epitope peptides derived from survivin, each interacting specifically with a different HLA molecule and having at least one of the following characteristics:

(i) capable of binding to the Class I HLA molecule to which it is restricted at an affinity as measured by the amount of the peptide that is capable of half maximal recovery of the Class I HLA molecule (C_{50} value) which is at the most 50 μM as determined by the assembly binding assay as described herein,

(ii) capable of eliciting INF-γ -producing cells in a PBL population of a cancer patient at a frequency of at least 1 per 10^4 PBLs as determined by an ELISPOT assay, and/or

(iii) capable of *in situ* detection in a tumor tissue of CTLs that are reactive with the epitope peptide.

2. A pharmaceutical composition according to claim 1, wherein each epitope peptide interacts specifically with a MHC Class I HLA-A molecule, a MHC Class I HLA-B molecule or a MHC Class I HLA-C molecule.

3. A pharmaceutical composition according to claim 1 or 2, wherein said MHC Class I HLA-A molecule includes HLA-A1, HLA-A2, HLA-A3, HLA-A9, HLA-A10, HLA-A11, HLA-Aw19, HLA-A23(9), HLA-A24(9), HLA-A25(10), HLA-A26(10),, HLA-A28, HLA-A29(w19), HLA-A30(w19), HLA-A31(w19), HLA-A32(w19), HLA-Aw33(w19), HLA-Aw34(10), HLA-Aw36, HLA-Aw43, HLA-Aw66(10), HLA-Aw68(28), HLA-A69(28).

4. A pharmaceutical composition according to any of the preceding claims, wherein said MHC Class I HLA-B molecule includes any of the following: HLA-B5, HLA-B7, HLA-B8, HLA-B12, HLA-B13, HLA-B14, HLA-B15, HLA-B16, HLA-B17, HLA-B18, HLA-B21, HLA-Bw22, HLA-B27, HLA-B35, HLA-B37, HLA-B38, HLA-B39, HLA-B40, HLA-Bw41, HLA-Bw42, HLA-B44, HLA-B45, HLA-Bw46 and HLA-Bw47.

5. A pharmaceutical composition according to any of the preceding claims, wherein said MHC Class I HLA-C molecule includes any of the following: HLA-Cw1, HLA-Cw2, HLA-Cw3, HLA-Cw4, HLA-Cw5, HLA-Cw6, HLA-Cw7 and HLA-Cw16.

6. A pharmaceutical composition according to any of the preceding claims, wherein said epitope peptide is restricted to a MHC class I HLA species selected from the group consisting of HLA-A1, HLA-A2, HLA-A3, HLA-A11 and HLA-A24.

7. A pharmaceutical composition according to any of the preceding claims, wherein said epitope peptide is restricted to a MHC class I HLA species selected from the group consisting of HLA-B7, HLA-B35, HLA-B44, HLA-B8, HLA-B15, HLA-B27 and HLA-B51.

8. A pharmaceutical composition according to any of the preceding claims comprising an epitope peptide, which is a native sequence of survivin of a mammal species.

9. A pharmaceutical composition according to any of the preceding claims comprising an epitope peptide, which is derived from human survivin.

10. A pharmaceutical composition according to any of the preceding claims, comprising an epitope peptide selected from the group consisting of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 27, SEQ ID NO: 45 and SEQ ID NO: 66.

11. A pharmaceutical composition according to any of the preceding claims, wherein said epitope peptide is derived from the native sequence of survivin by substituting, deleting or adding at least one amino acid residue.

12. A pharmaceutical composition according to claim 11, wherein said epitope peptide has been modified by substitution of anchor positions but not at TCR contact residues.

13. A pharmaceutical composition according to any of claims 11 or 12, wherein said epitope peptide is selected from the group consisting of SEQ ID NO: 4, SEQ ID NO:5 (basis p8, l 22) SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 36, SEQ ID NO:38, SEQ ID NO: 39, SEQ ID NO: 57,

14. A pharmaceutical composition according to any of the preceding claims, wherein the said epitope peptides are capable of eliciting INF-γ -producing cells in a PBL population of a cancer patient at a frequency of at least 10 per 10^4 PBLs.

15. A pharmaceutical composition according to any of preceding claims, wherein the said epitope peptides are capable of eliciting INF-γ -producing cells in a PBL population of a patient having a cancer disease where survivin is expressed.

16. A pharmaceutical composition according to claim 15, wherein the cancer disease is selected from the group consisting of a haematopoietic malignancy including chronic lymphatic leukemia and chronic myeloid leukemia, melanoma, breast cancer, cervix cancer, ovary cancer, lung cancer, colon cancer, pancreas cancer and prostate cancer.

17. A pharmaceutical composition according to any of the preceding claims, comprising an epitope peptide which is post-translationally modified.

18. A pharmaceutical composition according to any of the preceding claims, comprising a phosphorylated peptide.

19. A pharmaceutical composition according to any of the preceding claims, comprising an epitope peptide, which comprises Thr34 of the native survivin disclosed in US 6.245.523.

20. A pharmaceutical composition according to any of the preceding claims, further comprising an immunogenic protein or peptide fragment selected from a protein or peptide fragment not belonging to or derived from the survivin protein family.

21. A pharmaceutical composition according to claim 20, wherein the immunogenic protein or peptide fragment not belonging to or derived from the survivin protein family is a protein, or peptide fragment hereof, involved in regulation of cell apoptosis.

22. A pharmaceutical composition according to claim 20 or 21, wherein the immunogenic protein or peptide fragment not belonging to or derived from the survivin protein family is Bcl-2 or a peptide fragment hereof.

23. A pharmaceutical composition according to claim 20 or 21, wherein the immunogenic protein or peptide fragment not belonging to or derived from the survivin protein family is a member of the IAP protein family or a peptide fragment hereof.

24. A pharmaceutical composition according to claim 23, wherein said member of the IAP protein family is ML-IAP.

25. A pharmaceutical composition according to any of claims 20, 21, 23 and 24, wherein the immunogenic protein or peptide fragment not belonging to or derived from the survivin protein family is selected from the group comprising SEQ ID NO:75, SEQ ID NO:76, SEQ ID NO:77, SEQ ID NO:78, SEQ ID NO:79, SEQ ID NO:80, SEQ ID NO:81, SEQ ID NO:82, SEQ ID NO:83, SEQ ID NO:84, SEQ ID NO:85.

26. A pharmaceutical composition according to any of the preceding claims comprising HLA class I and HLA class II restricted epitopes.

27. A pharmaceutical composition according to any of the preceding claims comprising an adjuvant.

28. A pharmaceutical composition according to any of the preceding claims, which is a composition for *ex vivo* or *in situ* diagnosis of the presence of survivin reactive T-cells among PBLs or in tumour tissue.

29. A multi-epitope vaccine comprising a combination of MHC Class I-restricted epitope peptides derived from survivin having at least one of the following characteristics:

(i) capable of binding to the Class I HLA molecule to which it is restricted at an affinity as measured by the amount of the peptide that is capable of half maximal recovery of

the Class I HLA molecule (C_{50} value) which is at the most 50 μM as determined by the assembly binding assay as described herein,

(ii) capable of eliciting INF-γ -producing cells in a PBL population of a cancer patient at a frequency of at least 1 per 10^4 PBLs as determined by an ELISPOT assay, and/or

(iii) capable of *in situ* detection in a tumor tissue of CTLs that are reactive with the epitope peptide.

30. A multi-epitope vaccine according to claim 29, which includes a combination of survivin-derived peptide epitopes depending on the tissue type of the given patient.

31. A multi-epitope vaccine according to claim 29 or 30, wherein the vaccine is capable of eliciting an immune response against a cancer disease where survivin is expressed.

32. A multi-epitope vaccine according to claim 31, wherein the cancer disease is selected from the group consisting of a haematopoietic malignancy including chronic lymphatic leukemia and chronic myeloid leukemia, melanoma, breast cancer, cervix cancer, ovary cancer, lung cancer, colon cancer, pancreas cancer and prostate cancer.

33. A multi-epitope vaccine according to any of claims 29 to 32, wherein the vaccine elicits the production in the vaccinated subject of effector T-cells having a cytotoxic effect against the cancer cells.

34. Use of a combination of peptides as described in any of claims 1 to 28 for the preparation of a medicament for the treatment of cancer in combination with conventional cancer treatment such as radiotherapy or chemotherapy.